

Erythropoietin (EPO)

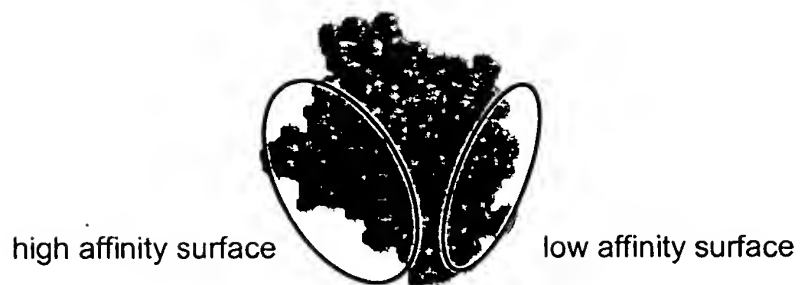


Fig. 2

The initial event is the association of the high affinity surface of an EPO molecule with the hormone binding pocket on an EPOR.

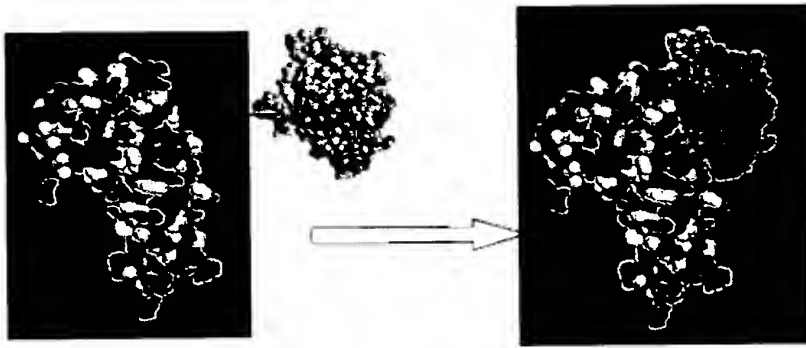


Fig. 3

The EPORs are anchored in the membrane, they can only diffuse laterally or rotate in the plane of the membrane.

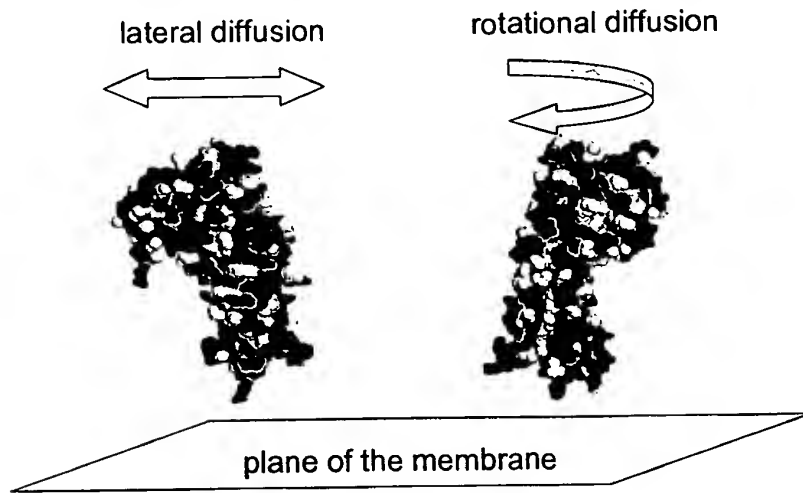
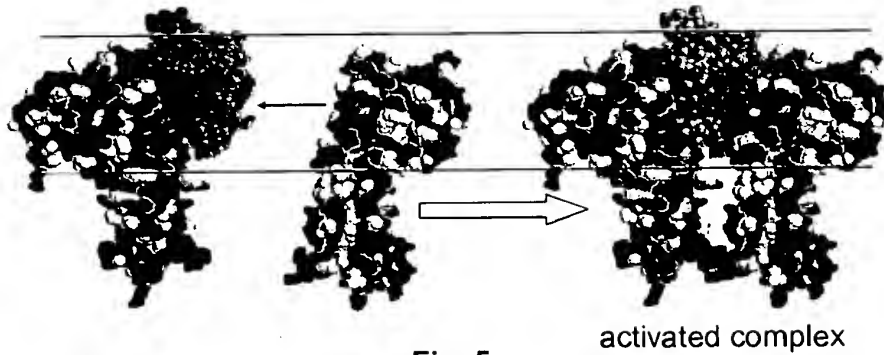


Fig. 4

Once the high affinity EPO surface binds to the first EPOR, the low affinity EPO surface is positioned within a narrow two-dimensional plane. Because the unoccupied EPORs can only diffuse laterally or rotate in that narrow plane, they can easily engage low affinity EPO surface, forming the activated complex.



LZHRs are short helical peptides with one face of the helix composed of the amino acid leucine (grey), which has a hydrophobic (water-avoiding) side chain.

When two LZHRs are in close proximity the two leucine-faces "zip" together (right), to be shielded from water.

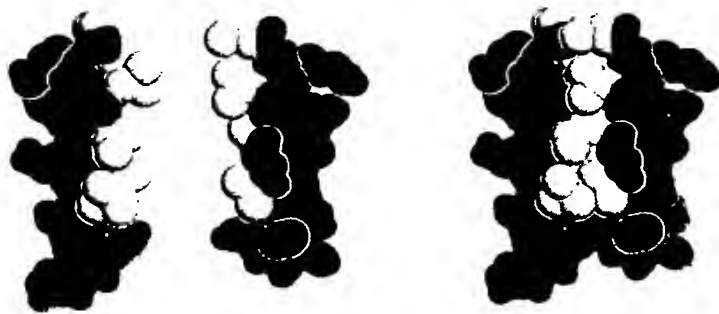


Fig. 6

By attaching a short LZHR to the EPOR by a flexible linker peptide, the formation of the EPOR*-EPO-EPOR* complex can be effectively achieved in a cell-free environment.

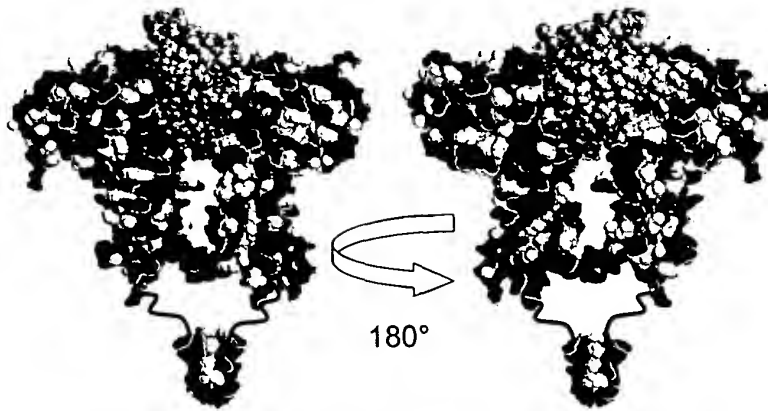


Fig. 7



FIGURE 8



FIGURE 9



FIGURE 10



FIGURE 11



FIGURE 12



FIGURE 13



FIGURE 14



FIGURE 15



FIGURE 16



FIGURE 17